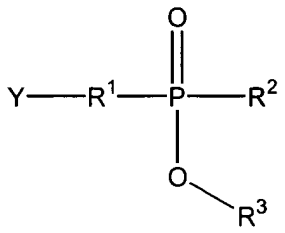
- -RELATED APPLICATIONS

This application claims priority based on U.S. provisional application no. 60/061,619, filed October 9, 1997, now expired, and from Germany patent application no. 197 45 628.6, filed October 10, 1997.- -

IN THE CLAIMS:

Please cancel claim 1, 10 to 15, without prejudice or disclaimer, and add the following new claims:

- - 16. A process for the preparation of chemical compounds of the formula (I)



(I)

in which

R^1 is an unsubstituted or substituted aromatic or heteroaromatic radical,

R^2 is hydrogen or an organic radical which may be linked to the rest of the compound of formula (I) by a hetero atom,

R^3 is hydrogen or an organic radical which is attached to a carbon atom and

Y is a functional group which is formed after the compound of formula (I) has been cleaved from the resin polymer in the last step of the process,

which comprises:

(a) reacting a resin-linker adduct of the formula (II)

$$[\text{resin polymer}] - [\text{linker} - Z - E^1 - S^1]_n \qquad \text{(II)}$$

in which

[resin polymer] is a radical of a resin which, in the resin-linker adduct (II) is connected via n binding sites with the n groups of the formula [linker-Z-E^1-S^1],

linker is in each case an organic linker,

Z is a linker-specific functional group or bond which, after cleavage of the compound (I) from the resin polymer, gives rise to the group Y in formula (I),

E^1 is defined as R^1 in formula (I) or is a radical which is suitable for preparing R^1 in compound (I),

S^1 is a functional group suitable for palladium-catalyzed substitutions analogous to the Heck reaction,

n is the number of the functional groups [linker-Z-E^1-S^1] at the resin, which depends on the molecular weight of the resin polymer and is greater than or equal to 1,

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in the presence of a suitable palladium catalyst with a compound selected from the group of the phosphinates (derivatives of hypophosphoric acid) of formula (III)

$$A^1\text{-O-(PHO)A*} \qquad \text{(III)}$$

in which

A^1 is hydrogen or an organic radical,

A* is a group which can be removed hydrolytically or after an intermediate reaction,

with substitution of the group S^1 to give a resin-bound compound of the formula (IV)

$$[\text{resin polymer}]\text{-}[\text{linker-Z-}E^1\text{-P(H)(=O)-O-}A^1\,]_n \qquad \text{(IV)}$$

in which A^1 is as defined in formula (III), and

(b) derivatizing, if appropriate, the compound (IV) in one or more further reaction steps at the organic radical E^1 to give a radical $(E^1)'$, thus yielding one or more resin-bound intermediates of the formula (IV)'

$$[\text{resin polymer}]\text{-}[\text{linker-Z-}(E^1)'\text{-P(H)(=O)-O-}A^1]_n, \qquad \text{(IV)}'$$

in which A^1 is as defined in formula (III), and

(c) hydrolyzing, if appropriate, the compound of the formula (IV) or (IV)' from step (a) or (b) to give a compound (V) or (V)'

$$[\text{resin polymer}]\text{-}[\text{linker-Z-}E^1\text{-P(H)(=O)-OH}]_n \qquad \text{(V)}$$

$$[\text{resin polymer}]\text{-}[\text{linker-Z-}(E^1)'\text{-P(H)(=O)-OH}]_n \qquad \text{(V)}'$$

and

(d) esterifying, if appropriate, the compound (V) or (V)' obtained according to (c) to give the compound of the formula (VI) or (VI)'

$$[\text{resin polymer}]\text{-}[\text{linker-Z-}E^1\text{-P(H)(=O)-O-}R^3]_n \qquad \text{(VI)}$$

$$[\text{resin polymer}]\text{-}[\text{linker-Z-}(E^1)'\text{-P(H)(=O)-O-}R^3]_n \qquad \text{(VI)}'$$

in which

R^3 is defined as R^3 in formula (I), but is not hydrogen, and

(e) reacting, if appropriate, a compound (IV), (V) or (VI) or (IV)', (V)' or (VI)' obtained according to (a), (b), (c) or (d), whose common structural feature is the phosphonous acid or phosphonous ester group, forming a phosphorus carbon bond, to give compounds of the formulae (VII) or (VIII) or (VII)' or (VIII)'

$$[\text{resin polymer}]\text{-}[\text{linker-Z-}E^1\text{-P}(R^2)\text{(=O)-O-}A^4]_n, \qquad \text{(VII)}$$

$$[\text{resin polymer}]\text{-}[\text{linker-Z-}(E^1)'\text{-P}(R^2)\text{(=O)-O-}A^4]_n, \qquad \text{(VII)}'$$

[resin polymer]-[linker-Z-E^1-P(E^2)(=O)-O-A^4]$_n$, (VIII)

[resin polymer]-[linker-Z-(E^1)'-P(E^2)(=O)-O-A^4]$_n$, (VIII)'

in which

R^2 is as defined in formula (I),

E^2 is an organic radical which can be derivatized to the radical R^2,

A^4 = A^1, H or R^3, and

(f) modifying the compounds obtained according to the abovementioned steps, if required, at the radicals E^1, (E^1)', E^2 and A^4 in such a manner that the resin bound compound of the formula (IX) is obtained

[resin polymer]-[linker-Z-R^1-P(R^2)(=O)-O-R^3]$_n$ (IX)

in which R^1, R^2, R^3 are as defined in formula (I), and

(g) cleaving the compound of the formula (I) from the resin-linker adduct of the formula (IX),

where in the formulae (IV) to (IX) and (IV)' to (VIII)' the radicals [resin polymer], linker, and Z are as defined in formula (II) and E^1 or (E^1)' in the formulae (V) to (VIII) or (V)' to (VIII)' are as defined in formula (IV) or (IV)'. - -

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In claims 2 to 9, line 1 in each claim, please replace "claim 1" with - -claim 16- -.

REMARKS

This invention relates to a combinatorial process for preparing chemical compounds of the following chemical scaffold

Y-R^1-P(=O)(-O-R^3)(-R^2)